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Prospective study on the role of C-reactive protein (CRP) in patients with an acute abdomen

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ABSTRACT

INTRODUCTION C-reactive protein (CRP) is used routinely in many hospitals to evaluate patients with an acute abdomen. We assessed CRP levels in non-specific abdominal pain (NSAP) and surgical conditions requiring operative or non-operative intervention. The aim of this study was to identify a level of CRP that can be useful in differentiating these three groups.

PATIENTS AND METHODS All patients older than 25 years and admitted with acute abdominal pain other than those requiring emergency surgery were included. CRP within 24 h was assessed in all patients. Various cut-off values (< 6, > 6–50, > 50–100, > 100–150 and > 150 mg/l) were used to identify a useful diagnostic level of CRP in the 3 groups.

RESULTS A total of 211 patients were prospectively evaluated – 129 women and 82 men with a mean age of 62.4 years (range, 27–92 years). CRP was performed in 196 within 24 h of admission. Sixty had NSAP while 136 had a surgical condition, of whom 69 had an operation/intervention while the rest were treated non-operatively. The median and interquartile (IQ) range for the three groups were: NSAP, 16 mg/l and 7.75–85.75 mg/l; surgical non-operative group, 75 mg/l and 30.5–150 mg/l; and surgical-operative, 111 mg/l and 42–212 mg/l, respectively. These results were statistically significant ($P = 0.001$). NSAP was diagnosed in 61% of patients at levels < 6 mg/l compared to 39% of patients in the surgical groups. At levels > 150 mg/l, NSAP was diagnosed in 15% of patients compared to only 54% and 31% for the operative and non-operative groups, respectively.

CONCLUSIONS Despite statistically significant differences between the three groups, no useful level of CRP could be identified to differentiate between patients with NSAP and those requiring operative or non-operative management.

KEYWORDS
C-reactive protein – CRP – Acute abdomen – Accuracy

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Clinical assessment remains the most important first step in evaluating patients with an acute abdomen. However, clinical examination has been found to be only accurate in 47–76% of patients with acute abdominal pain.[1–4] Even the most experienced surgeon will make correct diagnosis in only 4 out of 5 cases. This drops to 50% with junior doctors and doctors working in the community.[5] Delay in diagnosis may increase morbidity and mortality in these patients, many of them are elderly, and may have significant effects on hospital resources due to increased length of stay.

C-reactive protein (CRP) is a non-specific inflammatory marker that is used routinely in many hospitals as an aid in the diagnosis of patients with an acute abdomen. Most studies on the value of CRP in patients with an acute abdomen have focused only on acute appendicitis.[6–9] Few studies have assessed the diagnostic role of CRP in patients in the broad category of an acute abdomen. An elevated CRP level, even in isolation, can sometimes generate a cascade of complex investigations that may not necessarily answer the original question about why CRP was elevated in the first instance. Since CRP is a marker of inflammation, the aim of this study was to assess its role in differentiating three groups of patients. These were patients with non-specific abdominal pain (NSAP) and those presenting with definite surgical conditions requiring either operative or non-operative intervention.

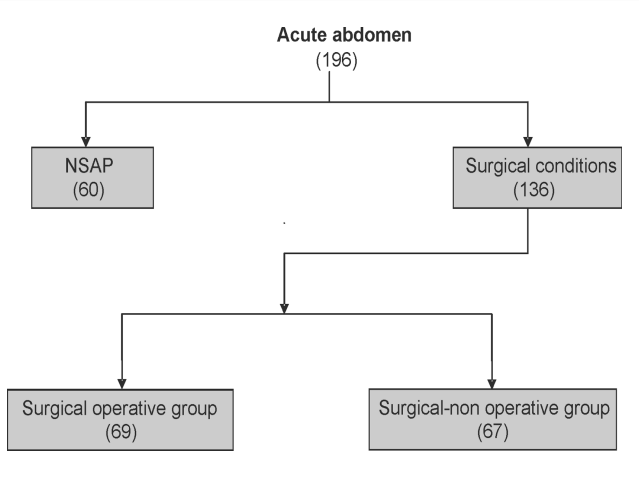

Figure 1 Diagnostic classification of 196 patients with an acute abdomen.

Patients and Methods

We prospectively evaluated patients admitted with non-traumatic, acute, abdominal pain to the surgical department of a large referral hospital over a period of 1 year from March 2003 to February 2004. All patients over 25 years of age admitted with acute abdominal pain were included in this study. Patients with obvious need for laparotomy and those with generalised peritonitis, mechanical bowel obstruction and leaking abdominal aortic aneurysm were excluded.

Data were entered on a structured proforma. Eligible patients were assessed and an initial diagnosis was made depending on a combination of history, clinical examination, laboratory tests and initial plain radiography. The final diagnosis was confirmed either at operation and subsequent histopathology when feasible or when further diagnostic tests confirmed the suspected diagnosis or indicated an alternative pathology. The laboratory method used to measure CRP in serum was polyethylene glycol (PEG) enhanced immunoturbidimetric assay. The CRP level within 24 h of admission was recorded and its diagnostic value compared to the final diagnosis of all patients. Patients were divided into three groups – those with NSAP, surgical condition requiring non-operative intervention, and surgical condition requiring operative intervention. To help identify a useful level of CRP that can differentiate the three groups, we divided the results into five sets using different arbitrary values. These were: levels < 6 mg/l (the normal laboratory reference value), > 6–50 mg/l, > 50–100 mg/l, > 100–150 mg/l and > 150 mg/l. These were compared for all three groups. The statistical method used to compare the three groups for significant differences were the Kruskal-Wallis and median tests as non-parametric tests to compare groups with continuous numerical data.

Results

A total of 211 patients fulfilled the inclusion criteria; 129 were females and 82 were males with a mean age of 62.4 years (range, 27–92 years). The admission, discharge and final diagnosis in all patients is shown in Table 1. CRP was performed within 24 h in 196 patients. Figure 1 shows the final patients' disposition in the three groups (NSAP,

Table 1 Admission, discharge and final diagnosis in 211 patients

Category	Admission diagnosis	Discharge diagnosis	Final diagnosis
Diverticulitis	72	49	47
Appendicitis	43	25	29
NSAP	11	5	63
Peritonitis	11	0	0
Bowel obstruction	10	1	5
Constipation	9	2	4
Mesenteric ischaemia	7	1	4
Perforated viscus	6	3	9
UTI	6	0	2
Cholecystitis/biliary colic	5	0	2
PUD	4	0	0
Pancreatitis	4	0	2
Abdominal mass	4	0	0
AAA	3	0	2
Intra-abdominal haemorrhage	3	1	1
Spigelian hernia	2	0	1
IBD	2	2	4
Ischaemic colitis	2	1	5
Incarcerated hernia	2	1	2
Psoas abscess	1	1	1
Ovarian cyst/mass	1	0	5
PID	1	0	1
Pneumonia	1	0	0
Anastomotic dehiscence	1	1	1
Colorectal cancer	0	4	7
Pyosalpinx	0	1	1
Hydrosalpinx	0	1	1
Clostridium difficile colitis	0	1	1
Pseudo-obstruction	0	1	1
Pancreatic cancer	0	1	1
Rectovaginal fistula	0	0	1
Acute on chronic colitis	0	0	3
Gastric sarcoma	0	1	1
Pyonephrosis	0	2	2
Adrenal mass	0	1	1
Dissecting aortic aneurysm	0	1	1

Table 2 Surgical conditions: non-operative treatment (n = 67)

Acute diverticulitis	42
Ischaemic colitis	5
Inflammatory bowel disease	4
Acute on chronic colitis	3
Ovarian cyst	3
Pancreatitis	2
Urinary tract infection	2
Sealed perforated viscus	1
Rectovaginal fistula	1*
Retroperitoneal haematoma	1
Pseudo-obstruction	1*
Clostridium difficile colitis	1
Pelvic inflammatory disease	1

*Original presentation with acute abdominal pain.

surgical conditions requiring non-operative or operative intervention). NSAP was the diagnosis in 60 patients and 136 patients had a definite surgical condition, of whom 69 underwent operation/intervention; the rest were treated conservatively (Tables 2 and 3).The sensitivity of CRP for all patients at the laboratory reference value for a positive test of > 6g/l was of 92.5% with a specificity of 23%. On the other hand, CRP was 34% sensitive and 85% specific at the arbitrary value of > 150 mg/l.

Table 4 shows the median and IQ range for all three categories. The results were statistically significant using the Kruskal-Wallis and median tests (P = 0.001).

The frequency of diagnosis of NSAP, surgical conditions requiring non-operative or operative intervention is shown in Table 5. Although 61% (14/23) those with CRP level < 6g/l had NSAP, 39% (9/23) had a definite surgical diagnosis, three of whom required emergency surgery. On the other hand, at levels > 150 mg/l, NSAP was the diagnosis in 15%

Table 4 The median and interquartile (IQ) range in the diagnostic groups

Group	Median	IQ range
NSAP	16	8–86
Surgical: non-operative	75	31–150
Surgical: operative	111	42–212

Values expressed in mg/l.
P = 0.001 (Kruskal-Wallis test).

Table 3 Surgical conditions: operative treatment (n = 69)

Acute appendicitis	26
Perforated viscus	8
Colorectal cancer	7*
Bowel obstruction	5
Diverticular abscess	4
Mesenteric ischaemia	3
Ovarian mass	2*
Pyonephrosis	2
Cholecystitis	2
Incarcerated hernia	2
Leaking AAA	1
Spigelian hernia	1*
Psoas abscess	1
Anastomotic dehiscence	1
Pyosalpinx	1
Gastric sarcoma	1*
Adrenal tumour	1*
Hydrosalpinx	1

*Original presentation with acute abdominal pain.

(8/54) of patients while only 54% (29/52) required emergency surgery/intervention and 31% (17/54) were treated non-operatively. At different CRP levels, there was no useful value to differentiate the three groups.

Finally, repeated CRP levels were performed in 39 of 60 patients with NSAP at the discretion of the treating surgeon. Twenty-two had increasing or persistently elevated CRP, 14 with dramatic decrease in CRP level and in three patients CRP remained normal. On the other hand, repeated CRP was performed in 85 of the 136 patients with definite surgical diagnosis; 70 had increasing or persistently elevated CRP, 12 with dramatic decrease in CRP and in three CRP remained normal.

Table 5 Distribution of NSAP, non-operative and operative surgical diagnosis at different CRP levels (n = 196)

CRP level (mg/l)	NSAP (n = 60)	Surgery: non-operative (n = 67)	Surgery: operative (n = 69)
< 6	14	6	3
> 6–50	27	21	19
> 50–100	8	14	11
> 100–150	3	9	7
> 150	8	17	29

Discussion

The acute abdomen remains a diagnostic challenge for even the most experienced surgeon. A whole range of different techniques including the use of structured data sheets, computer diagnosis, ultrasound, CT scanning and diagnostic laparoscopy have been used to improve the diagnostic accuracy.

CRP as a marker of inflammation is now routinely used in many hospitals in patients with an acute abdomen. However, most studies were conducted on patients presenting with suspected appendicitis with very few studies assessing the diagnostic role of CRP in acute abdomen especially those admitted to a surgical ward with a difficult clinical diagnosis. Two meta-analyses over the past 7 years studied the role of CRP in patients with suspected acute appendicitis. Hallan and Asberg[10] reviewed 22 eligible articles including 3436 patients on the accuracy of CRP in patients with suspected appendicitis. Sensitivity and specificity varied considerably from 40–99% and 27–90%, respectively; this was largely due to the use of different cut-off values for a positive test from 5–25 mg/l. They concluded that CRP is a test of medium accuracy and it was not possible to draw firm conclusion on its usefulness.[10] The reason for this conclusion is that only two of the 22 articles examined the question of whether CRP can provide significant independent information in the diagnosis of acute appendicitis and both confirmed this finding. However, both articles also found CRP to be a little inferior to the total leukocyte count. Most recently, Andersson[11] reviewed 28 different diagnostic variables in the assessment of patients with acute appendicitis in 24 eligible primary articles. The author found that each element of history, examination and laboratory markers of inflammation is of weak discriminatory and predictive capacity. However, a combination of more than one variable would make the diagnosis more likely. The most important diagnostic information was obtained from inflammatory markers, signs of peritoneal irritation (rebound tenderness, guarding and rigidity) and migration of pain.

This study confirms that CRP alone was not useful in differentiating a self-limiting condition like NSAP from other important surgical causes of acute abdomen where surprisingly high levels of CRP were found in patients who would have normally been treated as having NSAP. NSAP is a short-lived condition of unknown cause that otherwise settles spontaneously with no long-term consequences in the majority of patients at long-term follow-up. High levels of CRP in patients with NSAP may indicate that NSAP is actually an inflammatory condition. However, this adds little or nothing to the fact that such high levels of CRP cannot differentiate between this self-limiting condition and more potentially serious surgical diagnosis. We found no useful CRP value to differentiate between NSAP and other surgical conditions. More importantly, CRP was not able to differentiate between surgical conditions requiring surgery/intervention from those who were treated non-operatively.

Chi *et al.*[12] studied the role of CRP in 147 patients who attended the emergency department over a 2-month period with an acute abdomen. CRP levels were not known to the attending physician when making a decision about a patient's disposition from the accident and emergency department. They divided patients into two groups – group I (early discharge group) and group II (hospitalised or serious condition). In the group with a serious condition, the authors found that CRP was only 64% specific using a cut-off value for a positive test of > 5 mg/l. The authors concluded that CRP was a helpful aid in disposition decision making in patients with an acute abdomen.[12] However, this study was conducted over a short period of time and may have also included non-surgical patients which, though relevant to emergency physicians, may not reflect the true surgical patient population. There were no data on sensitivity and specificity of CRP levels in patients in group 1 (the early discharge group). Mean CRP levels in both groups were 11 mg/l and 61 mg/l, respectively. If CRP levels were not known to the attending physician at the time of disposition, this makes clinical decision alone an excellent method of patient disposition in their study group irrespective of CRP levels.

Our study shows that at low value for a positive test (> 6 mg/l), the specificity of CRP was very low at 23%. This reflects the finding that NSAP is a common diagnosis in our patient population. Repeated CRP levels in this study showed that 54% of patients with NSAP had increasing, or persistently elevated, levels of CRP when it was expected to be declining or even normal. Eriksson *et al.*[13] studied the value of repetitive CRP and white cell count in patients already considered for appendicectomy. They found that a normal value for both tests should be an indication to defer surgery, a conclusion which agrees with the meta-analysis by Andersson. However, looking at data from this study on CRP alone, we found that, in 224 patients, the admission CRP was only 55.4% specific and this did not improve on performing a second test (56.5% specific in 66 patients) and on performing the third test, where the specificity was only 62.5% in 30 patients.

Conclusions

Despite statistically significant results, there was no useful value of CRP that helps differentiate between the three groups of patients in this prospective study. CRP alone was not able to predict patients in the surgical groups who can be treated operatively or non-operatively. CRP value should only be considered in conjunction with other clinical and

biochemical parameters where the combination of one or more of these tests serve better to reach a correct diagnosis.

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